Inflammatory Dermatoses

Introduction

This lesson focuses on rashes that have an immune-mediated pathogenesis. They are nonoverlapping diseases, each with its own distinct illness script, specific sites where the rash is typically seen, and unique histologic findings. These diagnoses rarely require a biopsy in clinical practice. In the clinical sciences, the emphasis will be on recognizing and treating the rash. In the basic sciences, the emphasis is on recognizing the rash and knowing what the histology looks like, and how each disease alters the epidermis to cause the problem.

SKIN TERM	WHAT IT MEANS	WHERE YOU SEE IT
Hyperkeratosis	Enlarged stratum corneum	Calluses and psoriasis
Parakeratosis	Retention of nuclei in stratum corneum	Psoriasis
Hypergranulosis	Enlarged stratum granulosum	Lichen planus
Spongiosis	White space between keratinocytes	Eczema
Open comedones	Clogged pilosebaceous glands near surface	Acne, blackheads
Closed comedones	Clogged pilosebaceous glands not near surface	Acne, whiteheads

Table 6.1: Skin Terms to Diagnosis
Scary derm words and what they mean. Come back to this chart as you start each new diagnosis.

There are acute inflammatory dermatoses: urticaria, eczematous dermatitis, and erythema nodosum. There are chronic inflammatory dermatoses: psoriasis, seborrheic dermatitis, and lichen planus. Infectious dermatitis, such as occurs with acne, is discussed in MSK #17: *Appendages of Skin*.

Eczematous Dermatitis (Eczema)

Eczematous dermatitis is characterized by a **T-cell mediated** (type IV hypersensitivity) reaction that results in both edema in the stratum spinosum (**spongiosis**) as well as **hyperkeratosis** (and sometimes parakeratosis). The process is speculative, but begins with an antigen being encountered in the epidermis by epidermal macrophages (Langerhans cells), brought to CD4 T-helper cells in the local lymph node, and activating skin-homing CD4 cells to the site of that antigen. The T cells recruit other immune cells of varying kinds depending on which of the five types (which we are not teaching you) of eczematous dermatitis it is. The initial migration and cytokine release causes the patient to experience itchy erythema at the onset. After about a day, the proliferation takes hold, and a raised, scaling lesion appears at the site of the erythema (**scaling plaques**). There are five subtypes of eczematous dermatitis, but we want you thinking of all five as only inside (ingestion of food or medications) and outside (application of an antigen as in contact dermatitis).

The rash is **intensely pruritic, erythematous,** and **oozing**. Because the rash is so itchy, patients tend to scratch at it a lot. Acutely, scratching leads to **excoriations** (superficial abrasions). Chronically, in response to repetitive trauma, the skin undergoes secondary **lichenification** (diffuse epidermal thickening). In **children** the rash is found on **face and extensor surfaces** and is commonly encountered as new foods are started. As the patient ages, the rash tends to migrate to the **flexor fossae** (antecubital: elbows; popliteal: knees) as well as the **face and trunk**. Biopsies are not required, but if obtained, there will be spongiosis, hyperkeratosis, and parakeratosis. Treatment is with topical steroids for flares and to avoid precipitant antigens.

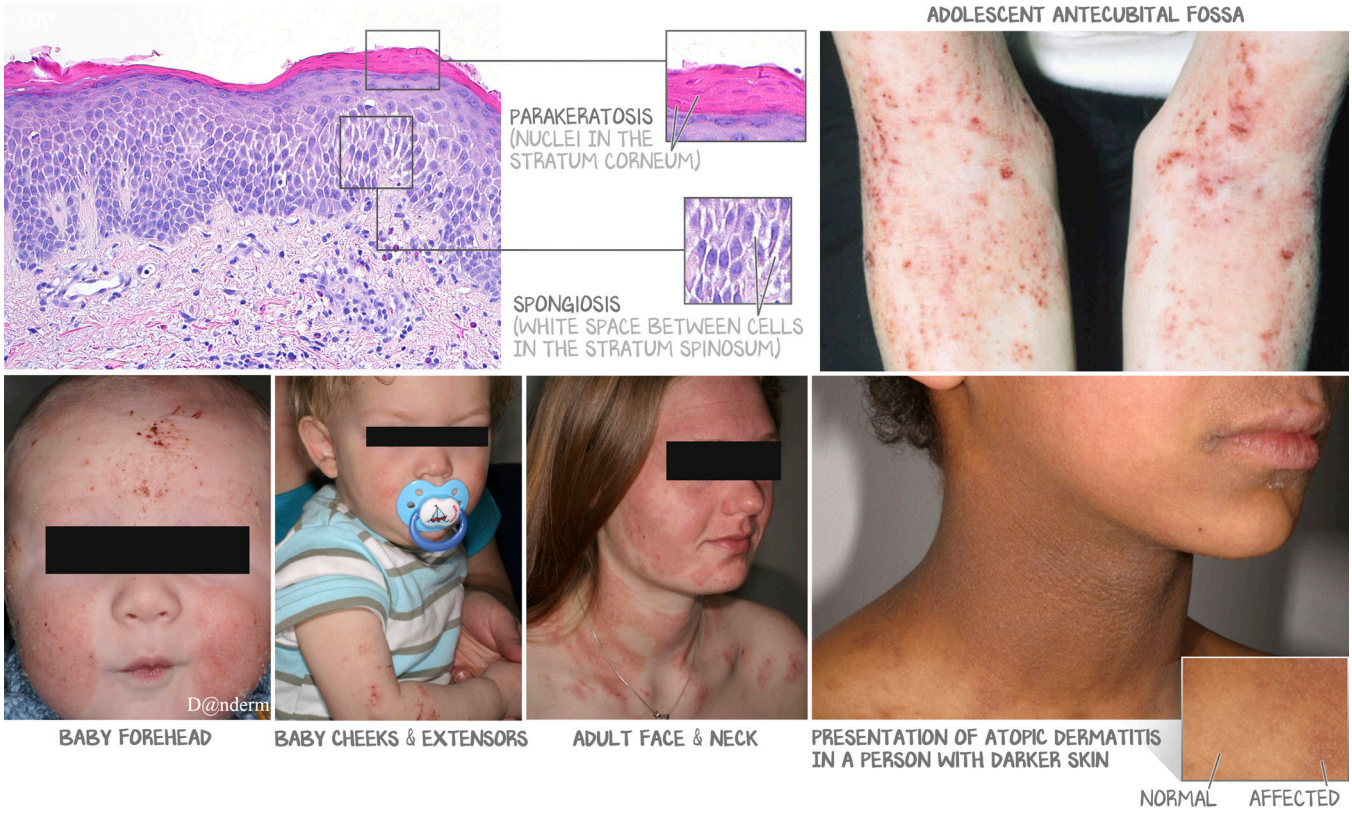

Figure 6.1: Eczema
Multiple examples of atopic dermatitis in babies (face and extensors), and in an adult and an adolescent (face and antecubital fossa), with an example of the rash in darker-skinned individuals (notice that it is not red). The histology demonstrates intraepidermal edema, termed spongiosis, which is excess white space between keratinocytes. Parakeratosis is also present in the stratum corneum (retained nuclei in the hot pink layer, which should be only terminally differentiated corneocytes without a nucleus).

Erythema Nodosum

There is limited understanding of the pathogenesis of erythema nodosum. It has been associated with the usual offenders that tend to cause autoimmune disease—strep infection, sulfonamides, oral contraception—and some cancerous and autoimmune associations—sarcoid, Crohn's, various collagen vascular disorders—but we don't have a solid understanding of its pathogenesis. It is expected to be a delayed hypersensitivity reaction as antigens deposit themselves in the **subcutaneous fat**. The normal process of acute inflammation happens—neutrophils arrive first, engulf baddies, summon for help then die in place; macrophages clear the field; fibroblasts scar the tissue. That inflammatory reaction in the subcutaneous fat raises the skin up. Erythema nodosum presents as an exquisitely **tender nodule** commonly occurring on the **shins**.

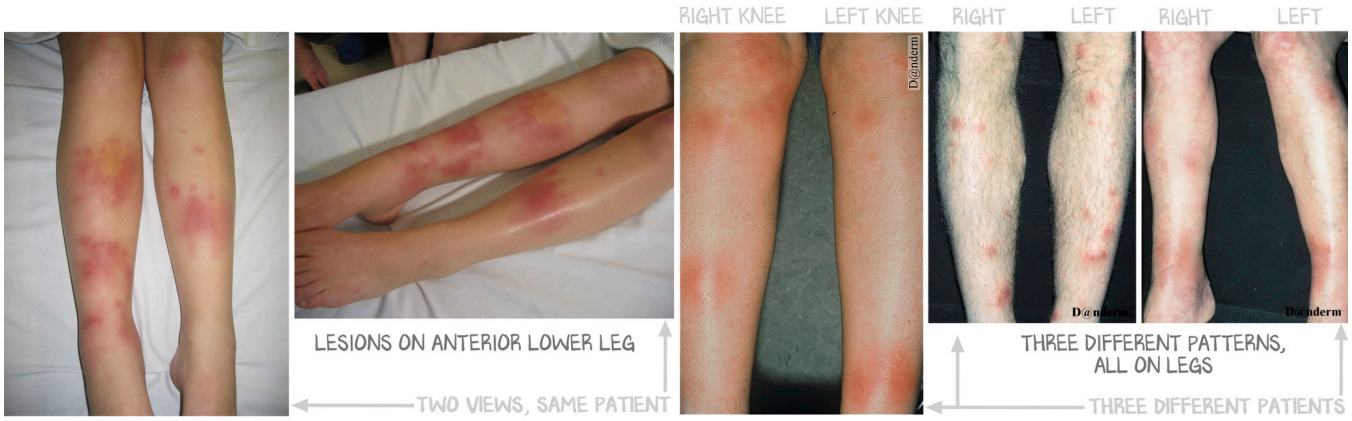

Figure 6.2: Erythema Nodosum
Multiple patients with erythema nodosum (EM). EM has a poorly understood pathogenesis and is a symptom of many autoimmune reactions (from drug reactions to acute strep infection, from sarcoidosis to Crohn's disease). It is not specific to any diagnosis, nor do we have a means of preventing it or treating it. It is usually self-limiting and short-lasting, and often does not accompany a flare of the associated disease. Although it doesn't always occur on the shins, involvement with the "ventral distal lower extremity"—the shins—is most commonly taught about the syndrome.

Psoriasis

Psoriasis can become overly complex if you let it. We try to turn it down to a manageable level.

Pathogenesis made easy. Think of psoriasis like this. Some signal induces the keratinocytes to proliferate excessively—both too many and too quickly. That happens only in the rete ridges, not only causing epidermal thickness to increase, but also elongating the rete ridges, making the epidermis above the rete ridges really deep. The dermal papillae elongate, too, making the epidermis above the papillae really shallow. The dermal papillae also get new capillaries. The keratinocytes are induced to proliferate, speeding up the growth of the epidermis. That means it takes less time for a new keratinocyte to reach the top of the epidermis. With less time to reach the apical surface, there is less time for the cells to do what they normally do—keratinize and degrade their nucleus. That means there are going to be mitotic divisions in the stratum spinosum (where there shouldn't be), keratinizing cells in the stratum granulosum (where they should be keratinized already), and retained nuclei in the stratum corneum (where there shouldn't be any).

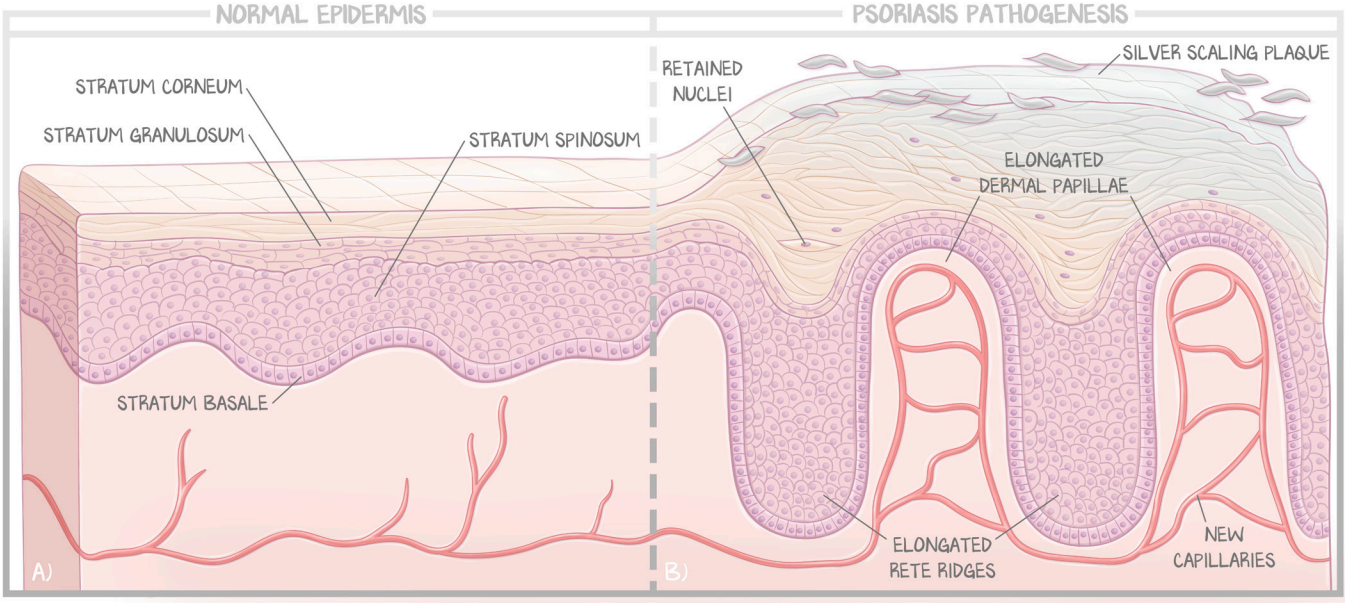

Figure 6.3: Psoriasis Pathogenesis
Normal epidermis with a stratum basale with mitosis, stratum spinosum with transcriptionally active nuclei, stratum granulosum full of keratinized cells, stratum corneum without nuclei, and normal-sized rete ridges and dermal papillae. Psoriasis shows elongated rete ridges and dermal papillae, mitosis in the stratum spinosum, a near-absent granulosum, and corneum with nuclei still in it. There are also new capillaries in the dermal papillae.

Patient presentation. Excess proliferation of keratinocytes leads to an **epidermal thickening** (acanthosis). Epidermal thickening means at the site of the lesion the epidermis will rise higher than the surrounding tissue, resulting in a raised **plaque** the patient can feel. The plaque is a **silvery scale** caused by abnormal shedding of the stratum corneum, a product of having nucleated cells in the corneum (parakeratotic corneum). Since the cells are pushed to the surface too quickly, they tend not to desquamate as quickly, resulting in **hyperkeratosis** (thicker corneum). It is the **silver scale** on an **erythematous base** (classically referred to as **salmon**-colored) that defines the lesion. It is found on **extensor surfaces** and the **scalp**. Psoriasis also affects the nails, causing **nail pitting** and **onycholysis** (separation of the nail from the nailbed). Those new capillaries in the dermal papillae, with relative thinning of the epidermis above the papillae, cause the **plaque to bleed** when the scales are picked (Auspitz sign).

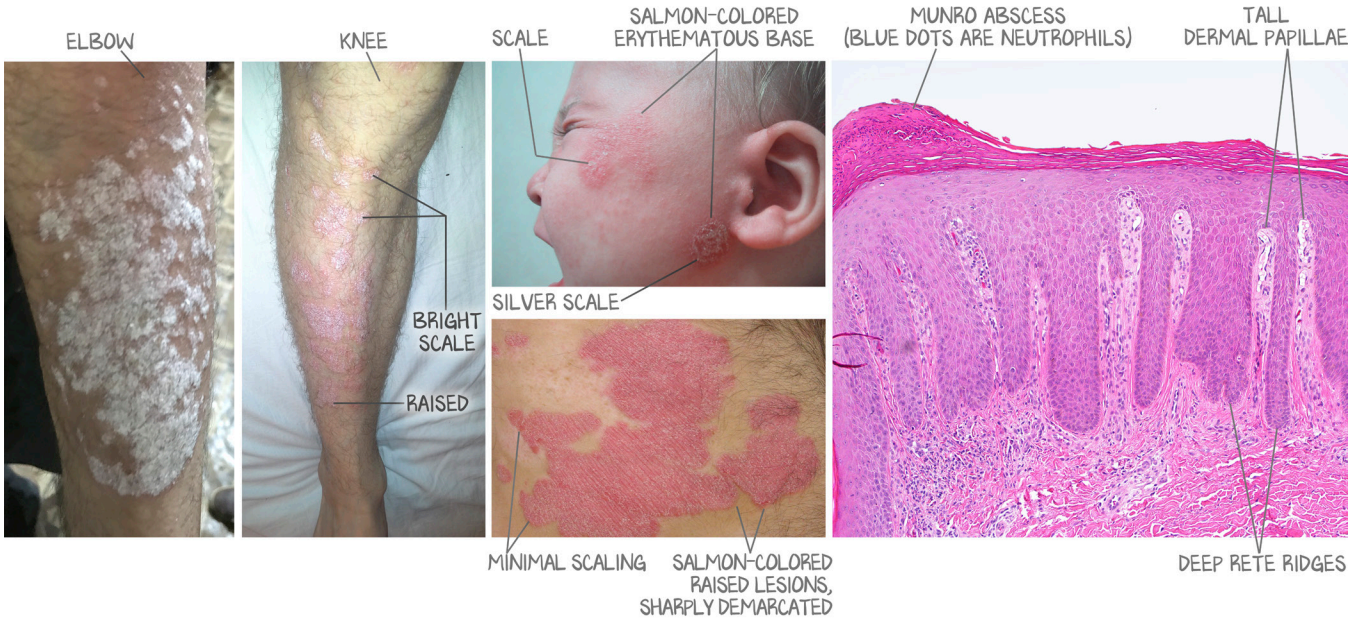

Figure 6.4: Psoriasis
Psoriasis rashes are characteristically salmon-colored, well-demarcated plaques that raise the adjacent normal skin. These plaques often scale, appearing silver over the salmon-colored plaque. The plaques have more variation than we are letting on (as shown in the photos above), but they all have the same fundamental salmon-colored raised skin. In adults, plaques tend to form on the extensor surfaces of hands, fingers, arms, legs, and neck. In kids, they tend to form on the face and flexors. Histologically, psoriasis characteristically has deepened rete ridges, which accommodate taller dermal papillae. There are no inflammatory cells in the dermis or epidermis. However, Munro microabscesses, collections of neutrophils in the stratum carenum, are a classic finding.

Histopathology. On histology there will be **epidermal thickening**, **elongated rete ridges**, and elongated dermal papillae. The **stratum spinosum** is **elongated,** the stratum **granulosum** nearly absent, and there are nuclei in the corneum **(parakeratosis**). The scales are caused by a thickened stratum corneum (**hyperkeratosis**). You can also get some neutrophils in there (this part we didn't have a chance to work into the story at the opening of this section). Neutrophils work their way through the spinosum (**spongiform pustules**) into the corneum, where they may form **Munro microabscesses**.

Seborrheic Dermatitis (SD)

Let's start off with why this disease follows psoriasis. While a biopsy is rarely necessary to make this diagnosis, if a biopsy were done, there would be **spongiosis** of the stratum spinosum, **hyperkeratosis**, **parakeratosis**, and the **presence of neutrophils**. Does that sound familiar? All of that was part of the histopathology of psoriasis. The lesions of SD are often described as **erythematous base** with yellow **scales**. Does that sound familiar? If you are not careful in a vignette, you may be duped by finding some of the words, but not all. In a real patient, when the person is in front of you, psoriasis and SD barely overlap. But enough of their words on the page do overlap that you might get tricked when taking an exam. Notice what is NOT in those descriptions? There is no elongation of the rete ridges, no elongation of the dermal papillae, no thinned granulosum, no involvement of the nails, and no bleeding when picked. There is just enough overlap to be confusing to the passing learner, but so much variation that if you master both diseases, you won't fall into a trap on test day.

SD is common, with 50 million Americans affected. Dermatologists would consider this next statement false, but because we know so little about the pathogenesis and use the same treatment for both diseases, we want you thinking that **seborrheic dermatitis is dandruff**. Dandruff is something you are very familiar with. When there is **white flaking** from the scalp, i.e., dandruff, we consider that mild SD limited to the scalp. When those white flakes are accompanied by **yellow scaling** on an **erythematous base**, or the lesions leave the scalp and are found elsewhere, we consider that moderate SD. When there is oozing, crusting, and superimposed bacterial infections, we consider that severe SD.

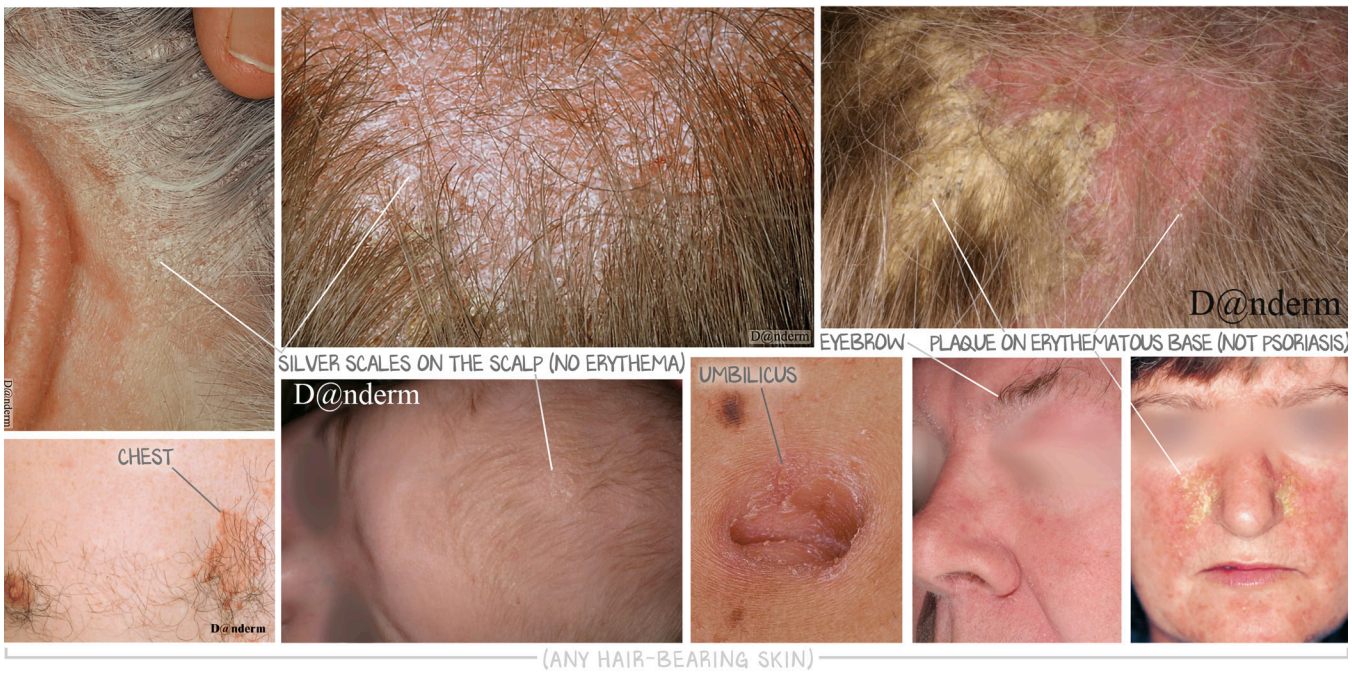

Figure 6.5: Seborrheic Dermatitis
Various presentations of seborrheic dermatitis, which can affect any region with hair-bearing skin. Most people are familiar with dandruff (adults) and cradle cap (babies), characterized by silver-to-white flakes, small scales, and pruritis. As the disease worsens, it can turn into a yellow plaque superimposed on an erythematous base. Unlike psoriasis, the yellow plaque does not scale, and the erythematous base does not have discrete edges.

SD occurs in **sebum-rich** regions of skin, where there is **thick hair**. While SD can occur anywhere on the body, it classically occurs on the **face**. In the **infant form**, known colloquially as cradle cap, there is the yellow scaling on an erythematous base localized to the scalp. In the **adult form**, the lesions may be found anywhere there is thick hair. For men, that means the scalp, eyebrows, and beard. For women, scalp and eyebrows.

In many instances SD is associated with ***Malassezia furfur*** infection and responds well to **selenium shampoo**. When the regular, over-the-counter dandruff shampoos you see on TV don't work, the treatment escalates. **Topical antifungal shampoos** (ketoconazole, miconazole) are used. For SD refractory to topical antifungals, it is assumed that even if the *Malassezia* is present, there is another **idiopathic inflammatory** cause. In these patients, aggressive immune modulation can be used, with DMARDs and even some biologics being attempted. Because that inflammation is idiopathic, you likely will not be tested on it.

Therefore, we want you learning that SD is dandruff, is caused by *Malassezia*, and is treated with selenium shampoo.

Lichen Planus

Lichen planus is the product of **hypergranulosis**—an enlarged stratum granulosum. This gives rise to the 6 P's—**p**ruritis, **p**urple/**p**ink (color counts as one P), **p**olygonal **p**lanar **p**apules, or **p**laques. Planar means flat-surfaced (not flat like a macule, but raised with an even surface). This is one disease that can affect the buccal mucosa, where you will see fine milky white streaks in a reticular pattern (**Wickham's striae**) or ulcerations. Lichen planus is associated with **hepatitis C infection**. Histology will reveal an enlarged stratum granulosum as well as **lymphocytic infiltrates** at the dermal-epidermal junction. This attacks that junction, leading to a **sawtooth** or **jagged** outline of the epidermis, with deep, narrow rete ridges penetrating into dermis. This is a disease that involves proliferation of its own layer (no other disease process involves the granulosum layer). But since we don't know that much about the pathogenesis, it doesn't get a lot of air time.

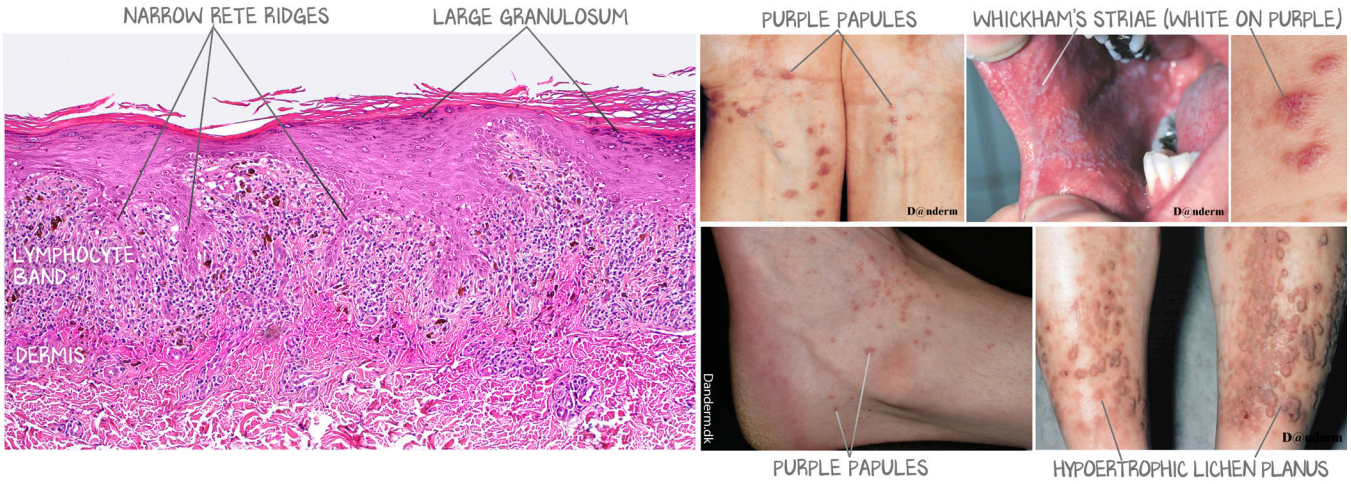

Figure 6.6: Lichen Planus
Histologically, lichen planus is characterized by a large band of lymphocytes below the basement membrane of the epidermis. This results in the autoimmune loss of epidermal cells, characterized by narrow rete ridges and inflammation, seemingly claiming what should be the epidermis. The size of the stratum granulosum is also increased. On the skin, lichen planus demonstrates discrete purple papules that can affect the skin or oral mucosa. Both skin and oral lesions can also present with a milky, lacy lining, called Wickham's striae.

DISEASE	NOTES
Atopic dermatitis	Filaggrin mutations, IgE and mast cells Intensely pruritic rash with excoriations (acute) and lichenification (chronic) Kids = rash on face and extensors Adults = rash on face and flexors Histology shows spongiosis; intraepidermal edema causes the plaque No change in the stratum sizes
Erythema nodosum	Poorly understood, acute inflammation in subQ space leads to fibrosis and granulomas Drug reaction (phenytoin, sulfur drugs, OCPs), autoimmune (Crohn's, sarcoid, others) Tender, erythematous nodules on shins
Psoriasis	T-cell mediation proliferation of keratinocytes Silvery scale on erythematous base that bleeds when picked; extensors and scalp Nail pitting, onychomycosis Spongiosis spinosum, elongated rete ridges, elongated dermal papillae, capillaries Hyperkeratosis, parakeratosis, neutrophils, Munro microabscesses
Seborrheic dermatitis	*Malassezia furfur*-induced dandruff (more severe forms idiopathic inflammatory) Infant: Cradle cap, yellow scales, erythematous plaque, scalp only Adult: White flakes (dandruff) to erythematous plaques with yellow scales that ooze; facial hair regions (beard, eyebrows, scalp) Selenium shampoo ⟶ Antifungal shampoo ⟶ Immune modulators
Lichen planus	Uncertain pathogenesis, associated with Hep C Pruritic, Purple, Polygonal Planar Papules, or Plaques (skin) Wickham's striae in the buccal mucosa (mucosa) Proliferation of stratum granulosum

Table 6.2: Summary Table
The diseases and high-yield facts from this lesson.

Citations

Figures 6.1, 6.4, 6.6: Courtesy of Jerad M. Gardner, MD.